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EXAMINER	
HADDAD, MAHER M	

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1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,049	DE KRETSER ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,10-12,17-19,23,24,26,30-32,34-36,39-41,46-48,52,53,55 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,8,9,13-16,20-22,25,27-29,33,37,38,42-45,49-51,54,56-58 and 60.

DETAILED ACTION

1. Claims 1-60 are pending.

2. Applicant's election with traverse of Group VII, claims 1-19, 23-26, 30-48, 52-55 and 59, drawn to a method of modulating the inflammatory response/therapeutically and/or prophylactically treating a condition, wherein modulating is downregulation of activin functional activity, achieved by introducing a proteinaceous molecule which functions as an antagonist of the activin expression product, wherein the antagonist is follistatin, and (i) airway inflammation as the specific condition; (ii) an acute inflammatory response; and (iii) targeting activin A, filed on March 16, 2009, is acknowledged.

Claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53,55 and 59 read on the elected species.

Applicant's traversal is on the grounds that the entire restriction requirement be reconsidered because the present application is a national phase application under 37 C.F.R.§ 371 and there is no disclosure in the '616 patent of a link between activin and inflammation. Still further, even the broadest method claims of the present application are directed to methods of modulating inflammation. The disclosure of the '616 patent, relating to a method of avoiding premature labour, is irrelevant to the present invention. This is not found persuasive because the claims recite the same products and the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the agent, i.e., human follistatin or a humanized antibody to activin, and the intended use thus impart no patentable weight on the claim (see MPEP 2111.02, section II). Accordingly, Applicant's inventions do not contribute a special technical feature when viewed over the prior art or the `616 patent they do not have a single general inventive concept and so lack unity of invention as set forth in the previous Office Action.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 4, 8-9, 13-16, 20-22, 25, 27-29, 33, 37-38, 42-45, 49-51, 54, 56-58 and 60 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

5. Claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53,55 and 59 are under examination as they read on a method of modulating the inflammatory response/therapeutically and/or prophylactically treating a condition, wherein modulating is downregulation of activin functional activity, achieved by introducing a proteinaceous molecule which functions as an antagonist of the activin expression product, wherein the antagonist is follistatin, and (i) airway inflammation as the specific condition; (ii) an acute inflammatory response; and (iii) targeting activin A.

6. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

8. Applicant's IDS, filed 10/26/06, is acknowledged.

9. Claims 5, 10, 17, 23-24, 30, 34, 39, 46, 52-53 and 59 are objected to under 37 CFR § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Even though these claims are in improper form, the examiner has chosen to examine claims.

10. 35 U.S.C. § 101 reads as follows:

> *"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".*

11. Claims 31-32, 34-36, 39-41, 46-48, 52-53, 55 and 59 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

12. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

13. Claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53,55 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 31-32, 34-36, 39-41, 46-48, 52-53, 55 and 59 provide for the use of modulators/follistatin, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

B. Claims 1-3, 5-7, 10-12, 17-19, 30-32. 34-36, 39-41, 46-48, 53 and 59 are being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the modulatory agent.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53,55 and 59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Claims 1-3, 5-7, 10-12, 17-19, 24 and 30 are directed to nebulous methods of modulating the inflammatory responses in a mammal. No agent is claimed to achieve the claimed modulation.

One cannot extrapolate the teachings of the specification to the scope of the claims because "modulating the inflammatory response" has mutually exclusive endpoints, i.e., modulating (inhibiting and inducing). The skilled artisan would not know whether the "modulator/agent" would inhibit or enhance pro-inflammatory cytokine mediated via activin. The skilled artisan would not know when the "modulator/agent" can be used to inhibit or when "modulator/agent" can be used to pro-inflammatory mediators mediated by activin. Those cytokine-modulating activities are mutually exclusive in that they reach opposing endpoints. It has not been shown that the "modulator/agent" is capable of functioning as that which is being claimed. The specification fails to show that "modulator/agent" including follistatin would either upregulate or downregulate activin, fragments, deriviative, mutants or variants thereof to a functional effective level. The specification on page 60, line 20 discloses that the peak release of activin A was unaffected by the administration of rhfollistatin-288. Yet applicant claims that it does.

Claim 2 recites a method of "prophylactically treating a condition or a predisposition to the development of a condition". However, the burden of enabling the prevention of a disease (i.e. the need for additional testing) would be greater than that of enabling a treatment due to the need to screen those mammals susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. Further, the specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to diabetic retinopathy within the scope of the presently claimed

invention. Nor is sufficient guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed follistatin in preventing airway inflammation state.

The claims recite activin or fragments, derivatives, mutants or variants thereof, however, the specification fails to show functional activities for the any activin, derivatives, mutants or variants thereof. It cannot be seen how to modulate the functional activity of activin, derivatives, mutants or variants thereof to of functionally effective level in said mammal. The specification fails to show that such derivatives, mutants or variants thereof exist in vivo and can be effective in inducing/inhibiting pro-inflammatory mediators. Moreover, the specification under Example 1 discloses that activin A was observed in mice following an injection of extracted LPS. No other activin has been associated with the LPS challenged mice. Yet the claims are drawn to any activin.

Claims 17-19 recite that the inflammatory responses is downregulation of the inflammatory responses such as TNFα, IL-1 and/or IL6. However, the specification under example 1 discloses that pretreatment with rhfollistatin-288 IL-6 peak concentrations were significantly increased in mice administred rhfollistatin-288 prior to LPS by approximately 2 fold.

The specification under Example 1 discloses the role of activin A in mice following an intraperitoneal LPS challenge, wherein a robust release of activin A was observed in the mice follwing an injection of re-extracted LPS. Follistatin was released into the circulation but was delayed compared to activin A. The level of IL-1β in the circulation were significantly lower than TNFα or IL-6 in LPS control mouse. In follistatin treated mouse, Activin A was unaffected. TNFα release was significantly suppressed. Il-6 was altered in bot absolute amounts and temporally. IL-6 peak concentrations were significantly increased in mice administered rhfollistatin-prior to LPS by approximately 2 fold. Release of IL-1β was not evident (see page 60, under Results). However, this data has implications for the role of Activin A in inflammatory response such as the sudden and dramatic release of the cytokines TNF-α, IL-1 and IL-6 produces the shock syndrome, leading to organ failure and death but unrelated to the claimed inflammatory responses of airway inflammation as claimed. LPS is a model effector of the acute phase response of bacteria. More importantly, the specification lacks showing that follistatin block the LPS-induced neutrophilic inflammation. Accordingly, the specification is not enabled for a method for treating inflammatory response occurs in the context of airway inflammation such as asthma.

The specification under Examples 2, pp. 61, discloses show the OVA sensitization and challenge model of allergic asthma highlights major changes in activin expression during the evolution of the pulmonary inflammatory response. The specification on page 61, discloses that the kinetics of activin secretion have been mapped finding that the peak concentration in BALF coincides with peak inflammation and eosinophila and the production of IL-4 using immunohistochemical analysis. Examples 3-6 on pages 62-67, provides prophetic examples, however, no actual data is presented. The specification under example 7 on page 68 discloses the changes in activin A/B during localized (CCL4-liver model) and systemic inflammation (LPS model). However no

profile of the mRNA expression in an airway inflammation model was conducted. Similarly Examples 8-10 deal with severe trumaic brain injury, LPS and healing of burns.

The specification on page 5, lines 7-9, discloses that Activin A, is now known to exhibit the pleiotrophic range of functional activities which are characteristic of most cytokines. The specification on page 6, lines 1-10, discloses that Activin affects the growth and differentiation of many cell types, stimulates the secretion of follicle-stimulating hormone from the pituitary gland and inhibits groth hormone, prolactin, and adrenocorticotropin release. However, activin A is now known to have many more properties besides this initial function for which it was first isolated. The specification on page 8, lines 3-14 discloses that the role of activin and follistatin in the context of inflammation, per se, has not been further elucidated, either in the context of their precise activities or in the context of the scope of the inflammatory conditions in which they function. In light of the extreme diversity in terms of the nature and extent of inflammatory responses which can occur, and the extremely pleiotropic activities of cytokines such as the various forms of activin, it is not surprising that the preliminary findings of the mid to late 1990's have not progressed in more substantial theories. Further, Activing A, activin B and follistatin are expressed by a wild variety of cell types and most organs in the body in response to a wide range of stimuli. The specification on page 8, lines 13-14 discloses that their role in the context of inflammation cannot be predicted and is therefor far from clear.

On the basis of the disclosed correlation of altered response to cytokine release in intraperitoneal LPS challenged mouse pretreated with human recombinant follistatin (see Example 1), applicant concludes that the scope of the soluble 288 amino acid residues follistan polypeptide encompassed by the claimed invention can have biological activity to modulate the inflammatory response in mammal and be provided as pharmaceutical compositions to subjects including human to effectively treat modulate inflammatory responses including inflammation occurs in the context of airway inflammation.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since there is no animal model system in the specification to treat airway inflammation such as asthma, interstitial lung disease, cystic fibrosis, lung transplantation, bronchiolitis obliterans, emphysema, COPD, sever acute respiratory syndrome, asbestosis, obstructive sleep apnoea, hyposia or pulmonary hypetension, it is unpredictable how to correlate intraperitoneal LPS challenged mouse results with downregulating activin to a functionally ineffective level in airway inflammation disorders in vivo clinical trial results. The specification does not adequately teach how to effectively treat airway inflammation such as asthma, interstitial lung disease, cystic fibrosis, lung transplantation, bronchiolitis obliterans, emphysema, COPD, sever acute respiratory syndrome, asbestosis, obstructive sleep apnoea, hyposia or pulmonary hypetension of and reach any treatment endpoint in individuals by administering follistatin. The specification does not teach how to extrapolate data obtained from intraperitoneal LPS challenged mouse studies to the development of effective *in vivo* treatment method, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the outcome of the follistatin exemplified in the specification.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

16. Claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53,55 and 59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of a method of modulating the inflammatory response in claimed claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53, 55 and 59. The claims provide a definition of a useful result rather than definition of what achieves that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention.

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "modulating the functional activity of activin" or "modulating the level of activin or fragment…" is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of being modulating activity/level of activin. It does not specifically define any of the proteins/nucleic acids/non-proteinaceous molecule/antibodies that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by the property of being "modulating" does not suffice to define the genus because it is only an indication of a general property the agent has. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than definition of what achieves that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate. "). There are insufficient relevant identifying characteristics disclosed.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms that are common to the genus. That is, the specification provides neither a representative number of species ((i) activin or fragments, derivatives, mutants

or variants thereof, (ii) proteinaceous or non-proteinaceous molecule (iii) follistatin functional fragments, derivative, homologue or mimetic thereof, or (iv) an agent capable of modulating the functionally effective level of activin)) to describe the claimed genus, nor does it provide a description of structural features that are common to species ((i) activin or fragments, derivatives, mutants or variants thereof, (ii) proteinaceous or non-proteinaceous molecule (iii) follistatin functional fragments, derivative, homologue or mimetic thereof, or (iv) an agent capable of modulating the functionally effective level of activin)). The specification provides no structural description of (i) activin or fragments, derivatives, mutants or variants thereof, (ii) proteinaceous or non-proteinaceous molecule (iii) follistatin functional fragments, derivative, homologue or mimetic thereof, or (iv) an agent capable of modulating the functionally effective level of activin) other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed molecules looks like. The specification's disclosure is inadequate to describe the claimed genus of agents/proteinaceous/non-proteinaceous molecules or fragments, derivatives, mutants or variants thereof.

Applicant has disclosed only rhfollistatin-288; therefore, the skilled artisan cannot envision all the contemplated agent possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53,55 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by US20030162715.

The ` 715 publication teaches follistatin-3 protein binds to activin in a dose-dependent manner in the above-described assay (see ¶5, 22, 85), wherein it binds to activin A and B (see ¶560&563). The `715 publication teaches the use of follistatin-3 polypeptides to treat disease. For example, patients can be administered follistatin-3 polypeptides in an effort to replace absent or decreased levels of the follistatin-3 polypeptide, to supplement absent or decreased levels of a different polypeptide, to inhibit the activity of a polypeptide, to activate the activity of a polypeptide, to reduce the activity of a membrane bound receptor by competing with it for free ligand, or to bring about a desired response (see ¶338). The `715 publication further teaches that follistatin-3 polynucleotides or polypeptides cam also be useful in treating autoimmune disorders (see ¶391). Examples of autoimmune disorders that can be treated include, but are not limited to: rheumatoid arthritis or Autoimmune Pulmonary Inflammation (see ¶392). Similarly, allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems, may also be treated by follistatin-3 polynucleotides or polypeptides (see ¶393). The `715 publication teaches that follistatin-3 polynucleotides or polypeptides, can also be used to modulate inflammation. For example, follistatin-3 polynucleotides or polypeptides can inhibit the proliferation and differentiation of cells involved in an inflammatory response. These molecules can be used to treat inflammatory conditions, both chronic and acute conditions, including inflammation associated with infection (e.g., septic shock, sepsis, or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine induced lung injury, inflammatory bowel disease, Crohn's disease, or resulting from over production of cytokines (e.g., TNF or IL-1.) (see ¶395). The `715 publication teaches a pharmacological composition of the invention use or sale for human administration (see ¶234, 235, 612).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the follistatin-3 polypeptide in the absence of evidence to the contrary.

The reference teachings anticipate the claimed invention.

19 Claims 1-3, 5-7, 10-12, 17-19, 23-24, 26, 30-32, 34-36, 39-41, 46-48, 52-53,55 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 03/006057.

The `057 publication teaches that the use of pharmaceutical compositions for the treatment and/or prophylaxis of disease associated with fibrosis in a vertebrate such as human (see page 2, line 21), said composition comprising at least one activin antagonist such as follistatin (see page 3, line 3), and optionally a pharmaceutically acceptable carrier, adjuvant and/or diluent. The invention also relates to methods of treatment of disease associated with fibrosis in a vertebrate (see abstract, page 21, lines 12-22 and claims 3, 5, 21, 26-28 in particular), wherein the disease associated with fibrosis is a pulmonary fibrosis, such as idiopathic pulmonary fibrosis or an interstitial lung disease (airway inflammation) (see page 3, lines 31-33). The `057 publication teaches that activin antagonist encompasses molecules that inhibit activin activity by binding to activin include follistatin (see page 12, lines 30-33).

Given that prior art methods, the product used in the reference methods are the same as the claimed method. The claimed functional limitations are considered inherent property of the claimed method.

The reference teachings anticipate the claimed invention.

20. No claim is allowed.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 28, 2009

/Maher M. Haddad/
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